pyridine for water determination and ethylene glycol for water determination (5:1) instead of methanol for water determination).

Residue on ignition Not more than 0.10% (1 g).

Assay Weigh accurately an amount of Cefituben and Cefituben Hydrochloride Reference Standard, equivalent to about 0.01 g (potency), dissolve each in 36 mL of 0.1 mol/L phosphate buffer solution for cefituben, pH 8.0, add exactly 4 mL of each of the internal standard solution, shake, and use these solutions as the sample solution and the standard solution. Perform the test with 5 μL of the sample solution and the standard solution as directed under the Liquid Chromatography according to the following conditions, and calculate the ratios, QT and QS, of the peak area of cefituben to that of the internal standard. Keep the sample solution and the standard solution at 5°C or below and use within 2 hours.

Amount [μg (potency)] of cefituben (C12H12N2O4S2) = amount [mg (potency)] of Cefituben Hydrochloride

Reference Standard × QT × 1000
QS

Internal standard solution—A solution of methyl p-hydroxybenzoate in acetonitrile (3 in 4000).

Operating conditions—
Detector: An ultraviolet absorption photometer (wavelength: 263 nm).
Column: A stainless steel column 4 mm in inside diameter and 20 cm in length, packed with octadehylicsilanized silica gel for liquid chromatography (7 μm in particle diameter).
Column temperature: A constant temperature of about 25°C.
Mobile phase: A mixture of 0.005 mol/L n-decyl trimethylammonium bromide TS and acetonitrile (4:1).
Flow rate: Adjust the flow rate so that the retention time of cefituben is about 10 minutes.

System suitability—
System performance: Dissolve 5 mg of Cefituben in 1 mol/L Hydrochloric acid TS to make 50 mL, and allow to stand for 4 hours at room temperature. To 10 mL of this solution add 0.1 mol/L phosphate buffer solution for cefituben, pH 8.0 to make 25 mL. When the procedure is run with 5 μL of this solution under the above operating conditions, trans-isomer and cefituben are eluted in this order with the resolution between these peaks being not less than 1.5.
System repeatability: When the test is repeated 6 times with 5 μL of the standard solution under the above operating conditions, the relative standard deviation of the ratios of the peak area of cefituben to that of the internal standard is not more than 1.0%.

Containers and storage Containers—Tight containers.
Storage—Light-resistant, and not exceeding 5°C.

Ceftizoxime Sodium
セフチゾキシムナトリウム

C12H12N2NaO4S2: 405.38
Monosodium (5R,7R)-7-[(Z)-2-(2-aminothiazol-4-yl)-2-methoxyiminoacetylaminol]-8-oxo-5-thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylate
[68401-82-1]

Ceftizoxime Sodium contains not less than 900 μg (potency) per mg, calculated on the anhydrous basis. The potency of Ceftizoxime Sodium is expressed as mass (potency) of ceftizoxime (C12H12N2O4S2: 383.40).

Description Ceftizoxime Sodium occurs as a white to light yellow, crystals or crystalline powder.
It is very soluble in water, sparingly soluble in methanol, and practically insoluble in ethanol (95).

Identification (1) Determine the absorption spectrum of a solution of Ceftizoxime Sodium (1 in 63,000) as directed under the Ultraviolet-visible Spectrophotometry, and compare the spectrum with the Reference Spectrum: both spectra exhibit similar intensities of absorption at the same wavelength.
(2) Determine the infrared absorption spectrum of Ceftizoxime Sodium as directed in the potassium bromide disk method under the Infrared Spectrophotometry, and compare the spectrum with the Reference Spectrum: both spectra exhibit similar intensities of absorption at the same wave numbers.
(3) Determine the spectrum of a solution of Ceftizoxime Sodium in heavy water for nuclear magnetic resonance spectroscopy (1 in 10) as directed under the Nuclear Magnetic Resonance Spectroscopy (H), using sodium 3-trimethylsilyl-propionate-d4 for nuclear magnetic resonance spectroscopy as an internal reference compound: it exhibits a single signal A at around δ 4.0 ppm, a multiple signal B around δ 6.3 ppm, and a single signal C at around δ 7.0 ppm. The ratio of integrated intensity of each signal, A:B:C, is about 3:1:1.
(4) Ceftizoxime Sodium responds to the Qualitative Test (1) for sodium salt.

Optical rotation [α]D 20° = +125 to +145° (0.25 g calculated on the anhydrous bases, water, 25 mL, 100 mm).

pH Dissolve 1.0 g of Ceftizoxime Sodium in 10 mL of water: the pH of the solution is between 6.0 and 8.0.

Purity (1) Clarity and color of solution—Dissolve 1.0 g of Ceftizoxime Sodium in 10 mL of water: the solution is clear, and colorless to light yellow.
(2) Heavy metals—Proceed with 2.0 g of Ceftizoxime Sodium according to Method 2, and perform the test. Prepare the control solution with 2.0 mL of Standard Lead Solution (not more than 10 ppm).
(3) Arsenic—Prepare the test solution with 2.0 g of
Ceftriaxone Sodium according to Method 3, and perform the test using Apparatus B (not more than 1 ppm).

(4) Related substances—Dissolve 0.11 g of Ceftriaxone Sodium in 100 mL of 0.1 mol/L phosphate buffer solution, pH 7.0, and use this solution as the sample solution. Perform the test with 5 μL of the sample solution as directed under the Liquid Chromatography according to the following conditions, and calculate the areas of each peak by the automatic integration method: each peak area other than ceftriaxone is not more than 0.5% of the peak area of ceftriaxone, and the total peak areas of all other substances than ceftriaxone is not more than 1.0% of that of ceftriaxone. **Operating conditions**

Detector, column, and column temperature: Proceed as directed in the operating conditions in the Assay.

Mobile phase: Dissolve 2.31 g of disodium hydrogenphosphate 12-water and 1.42 g of citric acid monohydrate in 1000 mL of water, adjust to pH 3.6 with diluted phosphoric acid (1 in 10) or dilute sodium hydroxide TS. To 200 mL of this solution add 10 mL of acetonitrile.

Flow rate: Adjust the flow rate so that the retention time of ceftriaxone is about 12 minutes.

Time span of measurement: About 5 times as long as the retention time of ceftriaxone after the solvent peak.

**System suitability**

Test for required detection: Pipet 1 mL of the sample solution, add 0.1 mol/L phosphate buffer solution, pH 7.0 to make exactly 100 mL, and use this solution as the solution for test for required detection. Pipet 1 mL of the solution, add 0.1 mol/L phosphate buffer solution, pH 7.0 to make exactly 10 mL, and confirm that the peak area of ceftriaxone obtained from 5 μL of this solution is equivalent to 7 to 13% of that of ceftriaxone obtained from 5 μL of the solution for test for required detection.

System performance: Dissolve about 0.01 g of Ceftriaxone Reference Standard in 100 mL of 0.1 mol/L phosphate buffer solution, pH 7.0, and use this solution as the solution for system suitability test. When the procedure is run with 5 μL of this solution under the above operating conditions, the number of theoretical plates and the symmetry coefficient of the peak of ceftriaxone are not less than 4000 steps and not more than 2.0, respectively.

System repeatability: When the test is repeated 6 times with 5 μL of the solution for system suitability test under the above operating conditions, the relative standard deviation of the peak areas of ceftriaxone is not more than 2.0%.

**Water** Not more than 8.5% (0.4 g, volumetric titration, direct titration).

**Assay** Weigh accurately an amount of Ceftriaxone Sodium and Ceftriaxone Reference Standard, equivalent to about 0.1 g (potency), and dissolve each in 0.1 mol/L phosphate buffer solution, pH 7.0 to make exactly 20 mL. Pipet 2 mL each of these solutions, add exactly 10 mL of the internal standard solution, then add 0.1 mol/L phosphate buffer solution, pH 7.0 to make 20 mL, and use these solutions as the sample solution and the standard solution, respectively. Perform the test with 5 μL each of these solutions as directed under the Liquid Chromatography according to the following conditions, and calculate the ratios, Q₁ and Q₉₅, of the peak area of ceftriaxone to that of the internal standard of each solution.

Amount [μg (potency)] of C₁₆H₁₆N₄O₂S₂

= amount [mg (potency)] of Ceftriaxone

Reference Standard × \( \frac{Q_1}{Q_S} \) × 1000

**Internal standard solution**—A solution of 3-hydroxybenzoic acid in 0.1 mol/L phosphate buffer solution, pH 7.0 (3 in 500).

**Operating conditions**

Detector: An ultraviolet absorption photometer (wavelength: 254 nm).

Column: A stainless steel column 4.6 mm in inside diameter and 25 cm in length, packed with octadecysilanized silica gel for liquid chromatography (10 μm in particle diameter).

Column temperature: A constant temperature of about 35°C.

Mobile phase: Dissolve 2.31 g of disodium hydrogenphosphate 12-water and 1.42 g of citric acid monohydrate in 1000 mL of water, adjust to pH 3.6 with diluted phosphoric acid (1 in 10) or dilute sodium hydroxide TS. To 450 mL of this solution add 30 mL of acetonitrile.

Flow rate: Adjust the flow rate so that the retention time of ceftriaxone is about 4 minutes.

**System suitability**

System performance: When the procedure is run with 5 μL of the standard solution under the above operating conditions, ceftriaxone and the internal standard are eluted in this order with the retention times of these peaks being not less than 7.0 and the symmetry coefficient of each peak is not more than 2.

System repeatability: When the test is repeated 6 times with 5 μL of the standard solution under the above operating conditions, the relative standard deviation of the ratios of the peak area of ceftriaxone to that of the internal standard is not more than 1.0%.

**Containers and storage** Containers—Tight containers. Storage—Light-resistant.

**Ceftriaxone Sodium**

セフトリアキソナトリウム

C₁₆H₁₆N₄O₂S₂·3½H₂O: 661.60

Disodium (6R,7R)-7-[(Z)-2-(2-aminothiazol-4-yl)-2-methoxyiminoceterylaminol]-3-(6-hydroxy-2-methyl-5-oxo-2,3-dihydro-1,2,4-triazin-3-ylsulfanymethyl)-8-oxo-5-thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylate hemiheptahydrate [104376-79-6]

Ceftriaxone Sodium contains not less than 834 μg (potency) per mg, calculated on the anhydrous basis. The potency of Ceftriaxone Sodium is expressed as mass (potency) of ceftriaxone (C₁₆H₁₆N₄O₂S₂; 554.58).